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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/762,294	04/02/2001	Chil-Yong Kang	9611-16	4835

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EXAMINER	
PARKIN, JEFFREY S	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 10/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/762,294	KANG ET AL.	
	Examiner	Art Unit	
	Jeffrey S. Parkin, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6,7 and 31-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 6, 7, 31-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

4.9

Detailed Office Action

37 C.F.R. § 1.114

A request for continued examination under 37 C.F.R. § 1.114, including the fee set forth in 37 C.F.R. § 1.17(e), was filed in this application after final rejection on 20 June, 2005. Since this application is eligible for continued examination under 37 C.F.R. § 1.114, and the fee set forth in 37 C.F.R. § 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 C.F.R. § 1.114.

Status of the Claims

Claims 1, 6, 7, and 31-40 are currently under examination. Applicants' submission filed on 20 June, 2005, did not contain any claim amendments or new arguments.

35 U.S.C. § 103(a)

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In

considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 1, 6, 7, and 31-36 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Li *et al.* (1994) in view of Daniel *et al.* (1992). Li and colleagues disclose the preparation of recombinant baculoviruses wherein the wildtype gp160 signal sequence has been replaced with the MSS or IL-3SS (see ABSTRACT, p. 256). This publication also discloses the preparation of recombinant Envs wherein the positive charge of the HIV-1 signal sequence has been reduced to contain no more than zero or one positively charged amino acids (see pp. 271-272). The preparation of *nef*-deficient avirulent viruses is not disclosed. However, Daniel *et al.* (1992) teach that *nef*-deficient SIV produces a virus that is replication-impaired and apthogenic. Furthermore, vaccine compositions comprising this virus protected macaques against viral infection. Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to prepare recombinant HIV-1 viruses with modified signal sequences, as taught by Li *et al.* (1994), and to further include a *nef*-deletion in the construct, as provided by Daniel *et al.* (1992), since this would provide a recombinant virus that is replication-impaired and expressed to high quantities. The skilled artisan would be motivated to prepare such a construct because of obvious

safety considerations (i.e., the virus would obviously be safer to handle in manufacturing viral antigens for diagnostic assays).

Claims 1, 6, 7, and 31-36 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Li *et al.* (1996) in view of Daniel *et al.* (1992). Li and colleagues disclose the preparation of recombinant baculoviruses wherein the wildtype gp160 signal sequence has been replaced with the MSS or IL-3SS (see ABSTRACT, p. 9606). The preparation of *nef*-deficient avirulent viruses is not disclosed. However, Daniel *et al.* (1992) teach that *nef*-deficient SIV produces a virus that is replication-impaired and apathogenic. Furthermore, vaccine compositions comprising this virus protected macaques against viral infection. Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to prepare recombinant HIV-1 viruses with modified signal sequences, as taught by Li *et al.* (1996), and to further include a *nef*-deletion in the construct, as provided by Daniel *et al.* (1992), since this would provide a recombinant virus that is replication-impaired and expressed to high quantities. The skilled artisan would be motivated to prepare such a construct because of obvious safety considerations (i.e., the virus would obviously be safer to handle in manufacturing viral antigens for diagnostic assays).

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 37-40 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are directed toward **vaccine** compositions for the prevention and treatment of HIV infection through the administration of a recombinant HIV-1 virus wherein the natural signal sequence has been replaced by a heterologous signal sequence.

The legal considerations that govern enablement determinations pertaining to undue experimentation have been clearly set forth. *Enzo Biochem, Inc.*, 52 U.S.P.Q.2d 1129 (C.A.F.C. 1999). *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988). *Ex parte Forman* 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). The courts concluded that several factual inquiries should be considered when making such assessments including the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965). The disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows:

1) The disclosure fails to provide adequate guidance pertaining to the correlates of protective immunity that are required for a protective or therapeutic immune response. In order to practice the claimed invention, the skilled artisan would require a knowledge of the correlates of protective immunity in order to assess if the vaccine composition of interest is producing the

desired immune response. However, the disclosure is silent concerning this aspect of vaccine development and it is not readily manifest what type of immune response (i.e., humoral, cell-mediated, or both) is required for protection and therapeutic immune responses.

2) The disclosure fails to provide adequate guidance pertaining to the quasispecies nature of HIV-1 infection. The vast genotypic and phenotypic diversity of HIV-1 means that any putative vaccine must be capable of neutralizing a number of different isolates, strains, and clades in order to be effective. However, the specification fails to provide any guidance pertaining to this subject.

3) The disclosure fails to provide any data from an art-recognized animal model demonstrating that the claimed vaccine compositions are truly effective vaccine immunogens. Before administering the claimed compositions, the skilled artisan would require a demonstration that said compositions were capable of inducing the desired immune response in the intended host.

4) The prior art teaches that HIV-1 vaccine development is extremely unpredictable (Haynes et al., 1996; Haynes, 1996; Burton and Moore, 1998; Letvin, 1998; Lee, 1997). To date there are no FDA-approved vaccines for the prevention or treatment of HIV-1 infection. This is due to several factors including the lack of understanding of the correlates of protective immunity, the lack of adequate animal models in which to assess vaccine efficacy, and the quasispecies nature of HIV-1 infection.

Accordingly, when all the aforementioned factors are considered *in toto*, it would clearly require undue experimentation from the skilled artisan to practice the claimed invention.

Correspondence

Any inquiry concerning this communication should be directed to

Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, James C. Housel, can be reached at (571) 272-0902. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-0908.

Applicants are reminded that the United States Patent and Trademark Office (Office) requires most patent related correspondence to be: a) faxed to the Central FAX number (571-273-8300) (updated as of July 15, 2005), b) hand carried or delivered to the Customer Service Window (now located at the Randolph Building, 401 Dulany Street, Alexandria, VA 22314), c) mailed to the mailing address set forth in 37 C.F.R. § 1.1 (e.g., P.O. Box 1450, Alexandria, VA 22313-1450), or d) transmitted to the Office using the Office's Electronic Filing System. This notice replaces all prior Office notices specifying a specific fax number or hand carry address for certain patent related correspondence. For further information refer to the Updated Notice of Centralized Delivery and Facsimile Transmission Policy for Patent Related Correspondence, and Exceptions Thereto, 1292 Off. Gaz. Pat. Office 186 (March 29, 2005).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

Jeffrey S. Parkin, Ph.D.
Primary Examiner
Art Unit 1648

02 October, 2005